Blair, James 2005

Dr. James Blair Oral History 2005

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James Blair Interview

December 12, 2005

Claudia Wassman: Today is Monday, December 12. My name is Claudia Wassman. I am doing an interview with Dr. James Blair.

James Blair: Greetings. Hello, good morning and good day.

CW: Okay. You came to the NIH In 2002. Maybe you can start with telling me a little bit about your career, and what brought you to the NIH.

JB: Okay, so previously I'd been at University College London In London, basically right really from when I was an undergraduate to being faculty. I never moved before. There were various different institutes at UCL I was attached to, but I was always attached to UCL in some capacity, and it had become time for a change. It was too embarrassing to be always at the same place, and the research possibilities here at NIH are so very good, I mean with the imaging facilities as well as the access to different types of patient populations. I was pretty limited in the UK to my primary interest, which is individuals with psychopathy, but here I can do that and then compliment that interest with conditions that are almost the opposite of psychopathy, such as Post Traumatic Stress Disorder (PTSD) or Generalized Anxiety disorder, so it was unique opportunities.

CW: What did you work on first in the UK?

JB: So in the UK, I was primarily working the neurocognitive impairments that give rise to the development of psychopathy, and with a specific emphasis on the idea that there's a [unintelligible] dysfunction in individuals with psychopathy. This prevents them appropriately responding to the sadness and fear of other individuals. This makes it very difficult for them to be socialized. Normal moral socialization involves teaching, or emphasizing the punishment value of the victim's distress, so the individual learns to avoid actions that hurt other individuals. These individuals don't have the same emotional response to the distress of other individuals, and therefore are less able to learn. Or either less able to find actions that cause other people pain deeply aversive, and therefore all other things being equal, if there are motivational reasons for why they should -- might want to offend, they will be more likely to offend, although obviously their pathology doesn't push people to offend, it just increases the probability, all other things being equal.

CW: And did you study adolescents?

JB: I studied both adolescents and adults, so really anybody over the age of eight and under the age of about 55, I was studying. In two separate parallel series of studies, though, there was the child, or rather adolescent series of studies, and then there was an adult series of studies. The children were all taken from schools for children with emotional and behavioral difficulties, both for comparison as well as the individuals with psychopathy. The adults were all taken from forensic institutions, both the individuals with psychopathy, as well as the comparison individuals.

CW: And how did you study them there? Did you do brain imaging on them over there?

JB: No, almost all the work I've done in the UK was behavioral work. There was some neuroimaging, but the neuroimaging there was on healthy individuals identifying the systems involved in the tasks that I've been taking behaviorally into the actual institutions that these people were based in. The possibility of doing imaging with the patient populations has really only emerged since I've been here.

CW: And was that also the reason that brought you to the NIH?

JB: That was certainly a major reason, yeah, yeah. No, no, the possibility of being able to do it. I mean it was just about possible in the UK, but incredibly difficult, whereas here it was incredibly difficult, but more than just about possible. It was possible to do, rather than only just possible.

CW: So what made it difficult?

JB: Well, I mean, there's always the patient risk issues. People worry but primarily in the UK there just wasn't very much time -- the facilities just weren't there. There was one scanner that lots of people were looking for time with, and I had no guaranteed access to that scanner. Here, as part of my, you know, post, I have guaranteed access to the scanner. Therefore, I can actually run the tasks that I've always wanted to, so it's another of the great advantages of being at NIH.

CW: That's great. So maybe you can say a little bit more about the program you have set up here.

JB: Effective Cognitive Neuroscience, yeah, so I mean basically it's the fundamental assumptions is the same as it was in the UK. What we're trying to identify is the neural regions involved in the different types of emotional processing. Not just characterize the neural regions, but also characterize what they actually do. How they actually do what they do by the way that they interact with other systems. So that's the sort of basic science approach, is trying to get at the neurocognitive architecture for emotion, and particularly different aspects of emotion that seem to be differently impaired in different patient populations. With respect to the actual patient populations, we've maintained an interest in individuals with psychopathy. I mean, the other exciting feature of being here is being able to work with other patient populations, and hopefully, to be able to use the work with these different patient populations to inform the studies of these various different populations. So the work with PTSD patients nicely dovetails with that with individuals with psychopathy, because you frequently see, or almost always see that whatever task the individuals with psychopathy do badly in one particular way, relative to healthy individuals, the individuals with PTSD will do badly, or differently than healthy individuals in exactly the opposite way. So you can basically see the system working in the healthy individual, both behaviorally and in the scanner, and then you can also see perturbations of that same system in these two patient populations, one going one way in patients with psychopathy, and one going the other way with patients with PTSD. Of course, if we get a much better handle on the neurochemical side of things, and we do have some windows into that with PTSD, but no windows into that with psychopathy. In other words what we may be able to do is what we understand with the neurochemistry of PTSD, and see whether that can apply to psychopathy, and therefore have readymade effectively treatments for individuals for individuals with psychopathy based on inferences from the work with PTSD. And currently the disorder of psychopathy is regarded as completely untreatable, so obviously being able to find potential treatments would be -- is a major -- or at least agents that will help manage the disorder is a major goal.

CW: So when you say systems, what do you mean by systems?

JB: So, I mean in a brain level, the regions, and the way that they just talk in terms of a system with respect to, say, the amygdala, we might be talking in terms of systems for emotional attention, which would be really a reference to the way that the amygdala talks to regions of temporal cortex. Priming up neurons that effectively representing condition stimuli, and by doing so, suppressing the representation -- or neurons representing competing stimuli in the environment, so that you really attend to that emotional system. So it's not just talking about areas but really talking about systems in the way that areas talk to each other and the way that the amygdala talks to temporal cortex with respect to emotional attention is very different form the way the amygdala talks to medial [unintelligible] cortex, to guiding behavior whether you're going to approach or avoid a particular stimuli in the environment. That' s the other sort of fundamental assumption, rather than talking about an area, it's really talking about systems as the way the particular areas interact.

CW: And how are you able to study this?

JB: This is through functional imaging. The idea is that you're developing tasks that will specifically index the way the amygdala talks to temporal cortex or the way the amygdala talks to the medial orbitofrontal cortex. I mean obviously it's more complicated than that, because, you know, pretty well, most tasks that talk with the amygdala will talk to both temporal cortex and medial orbito-frontal cortex, but you're talking about designing a task that stresses one type of aspect rather than another.

CW: How would that look?

JB: So, I mean in a classic sort of emotional attention task would be -- I mean one task we have currently going involves people looking at faces on the screen, and superimposed on those faces are words, either in upper case or lower case, or either with multiple syllables, or only monosyllabic words. Basically you're looking -- the subject has a task to do, which is either to name the gender of the person, name whether the -- or respond with a button press whether the word is in upper lower case or monosyllabic or bisyllabic, and so you basically have different levels of task demands, and that allows different levels of emotional interference with the actual tasks. And so you'll see that the way the amygdala talks to the temporal cortex increases as the task demands get more reduced. So that will be a sort of illustration. A standard sort of decision making paradigm, or one related to, particularly to psychopathy and PTSD is something called the passive avoidance paradigm, where the subject is presented with individual stimuli on the screen and has to decide whether they want to approach, press a button, or not to those stimuli. Some of the stimuli are good, and if they press the button when those stimuli are on the screen, they'll receive a reward of points. Some of the stimuli are bad, and if they respond to when those stimuli on the screen, then they' ll lose points, so the persons learns that there is good stimuli out there and there is bad stimuli out there, and they should approach the good, and they should avoid the bad stimuli. In that sort of paradigm, as the subject learns the task, you get a very nice, tightly integrated signal between the amygdala and medial lower [inaudible], medial upper frontal cortex. They'll both fire in a stronger and more synchronous fashion when the subject has learned both to avoid the good as well as to avoid the bad. If he sees a good stimuli, and the system sees a good stimuli and has learned the task, then it will respond. It' s correctly responding on the task, then you'll see this nice amygdala and medial lower [inaudible] response, as well as you'll see the signal coming in when the subject sees a bad stimulus. We are assuming, we don't know yet, or at least know for patients with PTSD, what we're seeing is an augmented amygdala response to both of these signals, or what looks like both of these signals. So what we see in patients with PTSD is an augmented amygdala response to those emotional cues, and so the idea when the subject is performing the task is they start learning to avoid the good stimuli, which is completely and utterly not a good way of behaving, but what we're assuming is going on, is that they're learning the bad stimuli, the neurons. The amygdala, still firing to that bad stimulus when the good stimulus comes up, and therefore, you're getting contamination of the valent signal to the good stimulus, and so consequently, what they're doing is basically, because of their contamination, they start learning to avoid the bad. They start associating the bad with the good stimuli, and you know, they become progressively more likely to avoid the good stimuli as they go through the task, although what their learning with the bad stimuli is intact. Individuals with psychopathy are exactly the opposite. With the good stimuli, they're quite good at always remembering to respond to the good stimuli. With the bad stimuli, they just cannot remember whether they should or should not respond, and so you'll see a better chance for performance with the good stimuli, and basically chance performance for the bad stimuli in individuals with psychopathy. Again, a complete opposite between those two sorts. We haven't taken that task in the scanner to the patients with psychopathy, only to the individuals with PTSD.

CW: So do you have any idea why that happens?

JB: As regards to fundamental causes? With PTSD, we know it's the trauma, I mean these people weren't like that before. So presumably there's something about the trauma that leads to a system where you're seeing the whole neural architecture of basic emotional processing heightened in responsiveness. The amygdala neurons fire to a weaker signal, they fire more strongly, and they fire for longer, and that leads to the assumption to the sort of contamination of valence, although, we're still obviously testing this. In the patients with psychopathy, we could be relatively confident it's not a simple trauma story, because if it was a simple trauma story, they should be looking like patients with PTSD. They should be having over responsive rather then under responsiveness in the amygdala. We know that they do have a lot of trauma in their history frequently, but again, if it was a simple trauma story, they should be looking like patients with PTSD, and they look, indeed, the complete opposite. There's now some beginning data to suggest there is a genetic basis to psychopathy. Presumably, there are genes that encode or influence the responsiveness of the neurons in the amygdala and associated structures, so that the individual is less able to respond to threat and other related stimuli that leads to problems with socialization, but we haven't confirmed the data suggesting a genetic influence has become a relatively strong. The way that that genetic influence is manifesting, we just don't know yet.

CW: How do you study it?

JB: Well, the knowledge of the genetic influence was from heritability studies from our group, and from now, two or three other groups out there looking. There used to be an unfortunate literature on the genetics of criminal behavior. The problem with that literature was that it sort of pretty explicitly assumed there were genes coding for individual criminal behaviors, which is obviously not -- it's just silly. We don't have any genes that code for our ability to mug or any other sort of antisocial behavior. But there is a considerable literature already suggesting that there is a genetic component to our emotional responsiveness and so what we were looking at was the heritability of the emotional component of psychopathy, this reduced emotional responsiveness, on the clinical assessment tool, and that's where you see this heritability component. That obviously just tells us there's a genetic component involved. It doesn't tell us which genes, and how they're affecting the brain but hopefully we'll resolve this over the next few years.

CW: So whom, at NIH do you remember? Those working on Post Traumatic Stress disorder and the biochemistry of it ?

JB: The PTSD work is done in conjunction with me and Eviva Lingham [spelled phonetically], who's another person with the mood and anxiety program. Danny Pine I collaborate with a lot for most of the patient work, so the adult work with patients with Generalized and Social Anxiety disorder is all done in collaboration with Danny Pine. The PTSD is, in part, a collaboration with him. The child work with individuals with psychopathy is done, again, in collaboration with Danny Pine, and to a lesser extent, with Ellen Leibenluft. I also have collaboration with Alex Martin in the LBC with more sort of basic science questions, you know, a couple of other collaborations here and there, but those are the sort of main ones.

CW: So can you say a little bit about the child studies? How old are the children that you look at?

JB: We're studying children from the age of 10 to 17, so quite a big range. We would be studying children younger than 10, but they're not -- they move too much on the scanner, so we've decided to have it cut off at ten, because that was the easiest -- the youngest we could really go and be reliably safe that the child would not move too much. I mean, other groups have worked with younger children than ten, but I think the conjunction of the types of children that we see and that, you know, most people don't go much beyond eight anyway, but we limit ourselves to 10, 10 to 17. Then there are children that -- they respond to adverts in the community, or parents respond to adverts in the community, talking about behavioral problems, and we assess them and see whether they show some of the emotional problems of psychopathy, or whether they're showing ADHD, or some other sort of problem.

CW: So you say that future possible [inaudible] treatment?

JB: Well, I mean, at the moment, we -- yeah, I mean this is obviously the goal, because we have no treatment for these individuals. They cause much distress to the parents and some of the people around them, and because of the nature of the emotional problem, they cannot experience all of the sort of emotional repertoire that a healthy individual has, so even for the individual involved, it's really not a desirable situation to be in. I mean you know you hear people saying how much they'd like to not have any guilt, but the fact is, given the additional problems they'd be faced with by not having guilt, they probably wouldn't if they really realized the full implications of having these sorts of problems. And so, but at the moment, that work is -- at the moment, what we're hoping to do is run studies to understand the neurochemistry of the systems that we've been identifying through the patient work. So looking at this work with healthy individuals and hoping that that will then inform us to what will be useful pharmacological agents, but we're not doing any treatment studies at the moment with this population. I mean I'm hoping we will in the not too distant future, but we're not right now.

CW: But can you do that?

JB: Certainly. I mean we're involved in a treatment study with patients with Social Anxiety disorder where we've been looking at the neural response to specific types of things. Tasks that we've identified these patients have problems with. We'll be looking at their performance before treatment and then after treatment, and seeing whether the actual situation is rectified, so yes, certainly. You can do it behaviorally; you can do an FMRI. There's lots of ways of doing it.

CW: How do you judge the importance of FMRI for the work that you are doing? Obviously it's very important, but then there are all of these scientists that wouldn't know what they're measuring so could you comment on the technique?

JB: You are measuring blood flow in the brain related to task activity. It's true that it's not a one to one mapping with neural responses, but to be honest, I read a considerable amount of the animal literature, where obviously people are directly measuring the neural responses, and I have done, and probably will do here again with lesion cases, with human lesion cases. So if you identified, using FMRI, that region X is involved in a particular task. Then you can see as well that an animal is doing something similar, or indeed the same task and will employ region X, and also you can then find patients with lesions to region X, and also they can't do the task, then you're pretty sure that region X is involved. Would I only use FMRI in the absolute absence of any other technique? Then, no, it does need to be complimented by other techniques. But then, all other techniques need to be complimented by other techniques. I have found it extremely useful. The worries about FMRI only really apply to the use of FMRI in the absence of any other scientific tool. If you' re using it in conjunction with other scientific tools, then most of the worries just go away.

CW: I had the impression that the use of FMRI really changed the understanding of emotion. Is that true?

JB: That's probably true. I think it was a complication of things, where people just ignored it generally, in the behavioral work. There wasn't really an FMRI work but the behavioral work had pretty well ignored emotion for absolutely ages. The Neuropsychology, well you never really saw a study of a patient with an amygdala lesion, you hardly saw reference to patients with orbitofrontal cortex lesions in the literature, but the FRMI was able to get at those systems and has transformed the work. I mean, it's difficult to see what was the primary contributor, but there's no doubt about it that FMRI has had an enormous impact in understanding emotion, absolutely enormous. I mean, having said that, many of the results were there in the animal literature, so it will be unfair to systems neuroscientists, animal-based systems neuroscientists to really say that the FMRI is completely revolutionary, because really, many of the results have been known with animals. They just were not known whether those results applied to humans, and FRMI has allowed us to be sure that those results do apply to humans. So it's been very important.

CW: Okay, great.

JB: That's all?

CW: That's it. Yeah.

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